NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Health Technology Appraisal

Cinacalcet HCl for the treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy

Scope

Remit / appraisal objective:
To appraise the clinical and cost effectiveness of cinacalcet hydrochloride for the treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy

Background:
People with chronic renal disease often suffer from secondary hyperparathyroidism. This disorder is characterised by persistently elevated levels of parathyroid hormone (PTH) and disturbances in phosphate and calcium metabolism. Clinical manifestations include vascular calcification and renal osteodystrophy with symptoms including bone, joint and muscle pain, and pruritus. There is an increased risk of fracture and cardiovascular disease.

In 2001 there were approximately 30,000 people in England and Wales receiving renal replacement therapy including approximately 15,500 on dialysis. The incidence and prevalence of renal impairment and established renal failure is expected to increase as the population ages and the prevalence of diabetes increases. Between 40 and 50% of patients on dialysis have PTH or phosphate levels outside the recommended range.

The goal of current therapies is to re-establish homeostasis of serum phosphate, PTH and calcium levels. Conventional therapy includes dietary modification, the use of calcium and non-calcium phosphate binders or vitamin D analogues, adjustments to the dialysis regimen, and calcium supplementation. The optimum combination of therapies for individuals changes over time and varies between patients. Some patients require sub-total parathyroidectomy.

The technology:
Cinacalcet HCl (Mimpara, Amgen Ltd) is an orally administered calcimimetic compound that increases the sensitivity of calcium-sensing receptors in the parathyroid gland. It inhibits the release of PTH within a few hours of administration, thus reducing serum calcium and phosphate. Patients who receive cinacalcet may need additional monitoring for calcium, phosphate and PTH levels compared with people who receive current standard treatments for renal failure.

Cinacalcet received its first marketing authorisation in October 2004 and was first launched in April 2005 in the UK. It is licensed for the treatment of secondary hyperparathyroidism in patients with end-stage renal disease on maintenance dialysis therapy. It is also indicated for the reduction of hypercalcaemia in patients with parathyroid carcinoma. The Summary Product Characteristics states that the safety and efficacy have not been established in people below the age of 18 years.

Intervention(s)	Cinacalcet HCl as an adjunct to current standard treatments
Population(s)	Adults with hyperparathyroidism secondary to renal failure
Current standard comparators	Standard management strategies not including cinacalcet If the evidence allows, a comparison may be made with surgical parathyroidectomy, only in the subgroup of patients with very high levels of parathyroid hormone in whom this may be considered an option.
Outcomes	Outcomes should include: • survival • incidence of fractures related to renal osteodystrophy • incidence of cardiovascular events • need for sub-total parathyroidectomy • symptoms such as bone pain and itching or mobility • hospitalisation • in the absence of directly measured mortality and morbidity outcomes, biochemical markers may be considered as potential surrogate outcomes • health-related quality of life • adverse effects of treatment • achievement of Renal Association standards for serum phosphate (below 1.8 mmol/L)
Economic analysis	The reference case stipulates that the cost

	effectiveness of treatments of cinacalcet should be expressed in terms of incremental cost per quality-adjusted life year. Treatment duration is unknown, but may be for life. The time horizon of the economic analysis should reflect the life expectancy of people with renal failure. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Conventional therapy includes dietary modification, alteration of the dialysis regimen and drugs such as phosphate binders and vitamin D analogues. These treatments may require adjustment after the addition of cinacalcet to the regimen. Guidance will be issued within the provisions of the marketing authorisation.